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COVID-19 v. Flu: A 'much more serious threat,' new study into long-term risks concludes

BY **CAROLYN BARBER**

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The new study found worse health outcomes in individuals months after their initial infection with COVID-19.

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Almost from the start of SARS-CoV-2's rampage around the globe, researchers and epidemiologists warned that it appeared to behave differently than known viruses, particularly seasonal flu. That included not only COVID-19's general contagiousness compared to flu viruses, but also its ability to cause clotting problems in the veins and arteries, result in loss of smell and/or taste, and even lead to a rare multisystem inflammatory syndrome in children.

That message was taken more or less seriously, depending on geography and, often, politics. But as a new study makes clear, the warnings have proved darkly prophetic.

The study, a comparative analysis with 18 months of follow-up of hospital admissions for those with COVID-19 and those with seasonal flu, found that COVID-19 patients experienced significantly higher rates of death, healthcare utilization, and ~~a~~dverse health outcomes in most organ systems than did patients with the flu. Its results were published on Dec. 14 in the infectious diseases section of the medical journal *The Lancet*.

'A multi-systemic disease'

"This was evident in pre-Delta, Delta, and Omicron (strains), and evident in both vaccinated and unvaccinated individuals," says Ziyad Al-Aly, the director of the Clinical Epidemiology Center, chief of research and development service at the Veterans Affairs Saint Louis Health Care System, and senior author of the study. "COVID remains a much more serious threat to human health than the flu."

The study arrives as the U.S. is seeing a significant uptick in COVID-related hospitalizations and with 15 states reporting high or very high levels of respiratory illness, which takes in COVID-19, the flu, RSV, and other respiratory diseases. The hospitalization numbers are well below those posted during Omicron's peak, but with colder weather moving more people indoors and into crowded settings, they may reasonably be expected to continue rising.

Al-Aly's study undertook a comparative analysis of 94 pre-specified health outcomes and found that over 18 months of follow-up, COVID was

associated with a "significantly increased risk" for 64 of them, or nearly 70%. The disease's enhanced risk list includes everything from cardiac arrest, stroke, chronic kidney disease, and cognitive impairment to mental health and fatigue, two characteristics often associated with long COVID.

By comparison, the seasonal flu was associated with increased risk in only six of the 94 conditions specified. Further, while COVID increased the risks for almost all the organ systems studied, the flu heightened risk primarily for the pulmonary(lung) system. Those findings, Al-Aly says, suggest that "COVID is really a multi-systemic disease, and flu is more a respiratory virus."

'A formidable foe'

Though COVID poses a greater risk, the seasonal flu should continue to be taken seriously, the researcher says. In fact, one clear finding of the study is that, much in the same way that long COVID is much more of a health problem than acute COVID, long flu poses more danger than does its acute phase.

"Five years ago, it wouldn't have occurred to me to examine the possibility of a 'long flu,'" Al-Aly says. "But a major lesson we learned from SARS-CoV-2 is that an infection which was initially thought to only cause brief illness can also lead to chronic disease. Conceptualizing the illness as an acute event obscures the much larger burden of health loss that occurs later. This revelation motivated us to look at long-term outcomes of COVID-19 versus flu."

The result: COVID-19 poses a much higher risk, both in the short run and long term, than flu. But the flu remains "a formidable foe," Al-Aly says. "Going into this winter season where cases of COVID and flu are rising, people should make sure they are vaccinated for both, and for RSV if they qualify, and take precautions to lower their risk."

According to the federal Centers for Disease Control and Prevention(CDC), nearly 80% of adult Americans have completed their primary series of COVID-19 vaccines, but only 17% have received a booster. Meanwhile,

nearly four in 10 adults had received a seasonal flu shot as of Nov. 25, the CDC estimated.

Roughly 15% of all U.S. adults have experienced long COVID symptoms, though figures range as high as the reported 34% in Oklahoma. According to a paper published earlier this year by Al-Aly's team in *Nature Medicine*, the physical fallout from long COVID may last two years or longer–and it can take a toll on the quality of life even for those whose initial cases didn't require hospital care.

'We trivialize COVID infections at our peril'

Clearly, long COVID remains a looming threat. Moreover, research shows that with each successive COVID-19 infection, we roll the dice. One can be young, healthy, and vaccinated, having experienced only mild symptoms during initial infections–then, almost inexplicably, develop long COVID on the next infection. Considering that long COVID can include conditions like memory loss, new diabetes, stroke, etc, and we have no proven treatments, the best strategy is to avoid it altogether.

Al-Aly's study mined the databases of the U.S. Department of Veterans Affairs to analyze data for more than 80,000 COVID-19 patients admitted to hospitals between March 2020 and June 2022, and for nearly 11,000 flu patients between October 2015 and February 2019. Up to 18 months of follow-up for participants was chosen "to comparatively evaluate risks and burdens of death" in addition to the pre-specified health outcomes, organ systems, hospital readmission, and admission to intensive care, the study says.

As part of their analysis, the researchers composited the health outcomes into 10 organ systems: cardiovascular, coagulation and hematological, fatigue, gastrointestinal, kidney, mental health, metabolic, musculoskeletal, neurological, and pulmonary. COVID-19 showed increased risk in nine of the 10, with the flu showing increased risk only in the pulmonary system.

The COVID group also had a higher risk of admission to intensive care in all of the time periods studied (30, 180, 360, and 540 days) versus the flu

group, as well as a higher risk of readmission to the hospital. And absolute rates of death, adverse health outcomes, and healthcare utilization, while high for both viruses, were "significantly higher for COVID-19 compared to seasonal influenza," despite changes in SARS-CoV-2 over time from pre-Delta to Delta to Omicron, the researchers said.

The study's authors noted two key limitations. First, the V.A. study population is predominantly older white males, which may limit the generalizability of the study's findings. And as the researchers assessed only people who were hospitalized with COVID or flu, the results should not be extrapolated to include non-hospitalized individuals.

Another strain of the virus, JN.1, has been detected. The growth advantage it appears to have over other variants suggests that it is either more transmissible or more capable of evading our immune systems. And the specter of long COVID hangs over each infection, to some degree or other. "We trivialize COVID infections at our peril," says Al-Aly. "The objective evidence is clear, whether it is a first infection or reinfection, COVID is still a serious threat to human health."

Carolyn Barber, M.D., is an internationally published science and medical writer and a 25-year emergency physician. She is the author of the book Runaway Medicine: What You Don't Know May Kill You*, and the co-founder of the California-based homeless work program Wheels of Change.*

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